

# **New Perspectives in Clinical Research: The Women's Cancer Research Foundation's Experience**

*by John P. Micha, MD; Cheri L. Graham, RN; Mark A. Rettenmaier, MD; John V. Brown III, MD; and Bram H. Goldstein, PhD*

## **Abstract**

The number of physicians involved in clinical research continues to decline. Financial and administrative barriers appear to be primarily responsible, although inadequate community-based infrastructure has also contributed significantly to this troubling phenomenon. Therefore, novel physician-friendly research models amenable to conducting efficient clinical research are necessary. The physicians from the Women's Cancer Research Foundation have developed such a paradigm over the past 23 years, which has proven to increase research productivity above and beyond the traditional academic model.

**Keywords:** clinical research, research infrastructure, nonprofit foundation

## **Introduction**

From 1985 to 2003, the percentage of physicians actively involved in research declined from approximately 5 to 2 percent.<sup>1</sup> Many community physicians consider research to be time consuming, tedious, and financially draining.<sup>2</sup> Consequently, even the physicians who enjoy clinical research are often dissuaded from this endeavor.

The traditional academic models are seemingly obsolete and have always been self-constraining, particularly since many of these research institutions contend that they are the ones who should determine how research is defined, the manner in which it is conducted, and the specific outcomes to be measured.<sup>3</sup> These conservative research paradigms are also encumbered by the evolving trends of teaching, research, and patient care.<sup>4</sup> Moreover, the research perceptions of clinicians, administrators, and researchers are often conflicting, further confounding any attempt at obtaining a consensus.<sup>5</sup> Consequently, academic research models have been hampered and become progressively more inefficient.<sup>6</sup>

In many academic medical research settings, physicians enrolled in fellowship programs, resident physicians in training, and medical students are critical to conducting clinical research.<sup>7</sup> However, unless there is consistent supervision from an experienced research physician and an appropriate research infrastructure is established, conducting substantive research studies may be extremely difficult. We raise this issue because many clinical fellows, residents, and medical students are not sufficiently trained in research methodology, nor do they have the experience to statistically analyze study data and subsequently write manuscripts for publication in peer-reviewed medical journals.

The majority of cancer patients are currently treated in the community setting and not at academic centers.<sup>8</sup> Evidence-based medicine requires clinical expertise and knowledge in accessing, interpreting, and applying the scientific results to communicate the different clinical outcomes with their patients.<sup>9</sup> Therefore, if the traditional academic research model desires a more progressive approach to conducting quality and evidenced-based research, then the importance of community-based physicians and experts should be considered.

Since evidence-based medicine is the standard to which physicians adhere, attracting more community-based physicians to clinical research should accelerate medical progress. However, the conventional “mom-and-pop” community physician offices do not typically possess the experience or research infrastructure to conduct substantive clinical studies. Thus, an ideal research model should satisfy the needs of both traditional academic medical institutions and community physician groups.

The Women’s Cancer Research Foundation (WCRF), a public nonprofit foundation, has created such a model in partnership with their gynecologic oncology medical practice. The WCRF’s basic tenet is to structure clinical research in accordance with a simple “turnkey” approach that entices interested physicians into conducting clinical research.<sup>10</sup> Their paradigm is based upon the belief that the predominant difficulty in conducting clinical research is not intrinsic to subject matter, but rather a result of reconcilable deficiencies in the research model and personnel description. The WCRF model posits that physicians should primarily be involved in roles that require senior or administrative clinical decision making and that the vast majority of the research process should be delegated to nonphysicians.

Initially, physician involvement is imperative to evaluate the prospects of novel therapies, innovative treatment devices, and patient outcome studies.<sup>11</sup> This may include several time-consuming meetings with senior biotechnology/pharmaceutical personnel and other clinical researchers to evaluate the proposed viability or efficacy of a new medication or device. However, most small community or academic medical offices may have great difficulty scrutinizing multiple and extensive study protocols, let alone writing original protocols, ensuring study eligibility, collecting and inputting patient data, conducting statistical analyses, and preparing a manuscript for journal publication.<sup>12</sup> Consequently, a diverse in-house research staff is necessary to address, manage, and accomplish the aforementioned functions.

## Description of Research Staff

A dedicated senior research nurse is imperative to coordinate and supervise all clinical studies.<sup>13</sup> This nurse can act as a research director, writing original protocols and negotiating contracts with limited physician supervision. Furthermore, he or she would also manage institutional review board (IRB) issues and maintain the Food and Drug Administration (FDA) Investigational New Drug (IND) application. Clinical nurses and medical assistants can conduct limited research, but when patient volume dramatically increases, they simply do not have sufficient time to manage both the clinical and research responsibilities.<sup>14</sup> Therefore, a separate senior research director and research team are necessary.

When a research group is operating multiple clinical trials concurrently, there should also be a designated number of trained clinical research coordinators working collaboratively with data managers and clinical nurses to organize data collection and trial management. Clinical research coordinators typically organize the initiation of a research study; recruit, screen, and enroll clinical study participants.. They also maintain drug accountability logs and constantly interact with study patients to ensure the accuracy of case report forms and regulatory documents.

A clinical research nurse can also expand his or her influence and resources during the supervision of multiple clinical trials via collaboration with trained medical assistants and data managers. When appropriately supervised, designated data managers and medical assistants can execute the daily responsibilities associated with study protocols.<sup>15</sup> Furthermore, they can frequently and comprehensively discuss a research protocol with the study participants and their family members, elucidating the significance of the trial and addressing corresponding questions and concerns.

Medical assistants and data managers, who are knowledgeable, detail oriented, compassionate, and able to multitask, can also screen patients and conduct extensive due diligence for prospective clinical

trials. Moreover, they can continually be relied upon to input and review study data, complete patient case reports, regularly inform and update the principal investigator and research nurses, respond to study monitor queries, and ensure that established study criteria are adhered to during all research phases.

When considering the methods of data collection, statistical analysis, and manuscript writing for journal publication, a PhD researcher trained in academic medicine can provide invaluable expertise.<sup>16</sup> Many clinicians do not have the time and often the experience to write peer-reviewed quality publications. While physician input is essential for a manuscript's development, quality, and review, the research paper can be primarily accomplished with a PhD organizing the specific details inherent in the project's preparation.

Significant research endeavors often require extensive hospital involvement in order to ascertain patient information and records. Thus, health information management (HIM) personnel can be invaluable resources to the research infrastructure.<sup>17</sup> The HIM department is an essential component to conducting quality research because HIM professionals are experts in the field of patient healthcare and medical information. They are certified health information specialists and are responsible for managing, documenting, interpreting, and tracking patients' medical records. Consequently, without their participation, most hospital-based research groups would be unable to effectively produce quality clinical research.

Clinical research requires accuracy and extensive knowledge of medical terminology. HIM professionals are specifically trained in these areas. Further, they employ advanced computerized encoding, document imaging, bar coding, and sophisticated transcription software to facilitate patient data and record processing. HIM professionals also ensure that collaboration with research groups is accomplished in accordance with strict federal HIPAA (Health Insurance Portability and Accountability Act) and state-mandated privacy laws and verify that confidential information and data are secure.

The duties of HIM professionals in the realm of research also include managing health records and medical information, coding diagnoses and reimbursement procedures, and ensuring quality control via information technology. Moreover, when attempting to assess the impact of research-related interventions on healthcare, HIM professionals can be instrumental in facilitating clinical study implementation, operation, and completion.<sup>18</sup> Since HIM professionals are experienced in many facets of research and are integral to the entire process, they would be highly qualified to perform the extensive duties of a clinical research coordinator and/or data manager for any research institution.

Many IRBs are hampered by bureaucratic issues; thus, the WCRF works solely with regional IRBs to decrease study approval time. This is essential because many traditional hospital-based IRBs require six to nine laborious months to permit initial study approval, whereas regional IRBs can often provide study approval in sometimes only a few weeks.<sup>19-21</sup> Furthermore, these regional IRBs are beneficial because they often comprise experienced reviewers who can provide valuable insight into protocol design.

Peer-reviewed publications are the gold standard of any research effort. Prominent national cancer centers like Cedars-Sinai Medical Center, MD Anderson Cancer Center, and Memorial Sloan-Kettering Cancer Center have significantly more gynecologic oncologists on staff than the WCRF physicians. Nevertheless, cumulative annual academic first-author manuscript production per physician at the WCRF exceeds that of these centers' gynecologic oncology divisions. This assessment was determined by calculating the average annual number of first-author gynecologic oncologist publications per institution, which was identified via [www.pubmed.gov](http://www.pubmed.gov) (see Figure 1).

The physicians in collaboration with the WCRF have produced nearly 40 peer-reviewed first-author publications (e.g., surgery outcome studies, case reports, and chemotherapy trials) in major medical journals from 2003 to 2007 (Table 1). This substantial manuscript production rate is an increase of over 320 percent compared to the previous 5 years wherein this new model was established. Fortunately for the WCRF, the physicians donate all of their research time. The doctors are willing to conduct research without financial remuneration because they recognize that in spite of their restricted time, clinical research is essential to advancing the field of medicine and improving overall patient care.

The tremendous increase in research efficiency has permitted three extremely busy gynecologic oncologists, all of whom annually perform approximately 1,200 surgeries, to collaborate with the WCRF research staff. This has resulted in the current enrollment and management of 14 large-scale patient clinical trials, two of which involved holding the FDA IND authorization. The trials comprise original investigator-initiated studies and industry-sponsored (e.g., pharmaceutical/biotechnology) studies, which have significantly increased the WCRF's annual amount of grant and public funding from \$276,000 in 2003 to \$565,000 in 2007 (see Figure 2).

Managed care also has significantly reduced the amount of funding necessary for clinical trials.<sup>22</sup> Therefore, charitable funding is necessary since the income from hospitals and biotechnology/pharmaceutical companies does not sufficiently cover operating expenses. This can be partially achieved through supportive patients and private-sector organizations. These individuals and organizations are likely to increase their financial involvement as they familiarize themselves with the practical aspects of relevant (i.e., personal) clinical research conducted at a designated institution.<sup>23</sup> In particular, WCRF patients and supporters are deeply involved in the organization, account for several of the development committee members, and plan the increasingly successful annual fundraisers.

## Discussion

Since traditional academic models are associated with significant frustration and inefficiency, employing the components of the WCRF paradigm (Figure 3) nationwide could significantly revolutionize clinical research productivity. While the model is hierarchical in design, the WCRF has been successful because the qualified research staff is cross trained and primarily familiar with nearly every aspect of the research process. Moreover, the individual researcher frequently participates in several facets of the design and management of a clinical trial, enabling him or her to acquire new skills and provide flexibility in order to achieve favorable results. For example, when the senior research nurse is unavailable to discuss a complicated research issue with a patient or study monitor, a data manager, HIM professional, or medical assistant would be able to intervene and appropriately address the scenario.

Individual research groups and conventional models could be easily modified to incorporate several features inherent in the WCRF paradigm. Community medical practices can also utilize the WCRF prototype or make adjustments amenable to their specific institution. The WCRF's successful research model facilitates physician involvement by providing more time for doctors to design, execute, and assist in conducting scientific studies without compromising their clinical responsibilities.

However, until the traditional academic research approach is critically evaluated and renovated, many of the practical and methodological issues will be difficult to reconcile. Therefore, we conclude that a progressive and judicious approach to conducting clinical research involves the development of a research team whose entire focus and viability is dedicated toward significant productivity and efficiency in the context of a nonprofit foundation model.<sup>24</sup>

John P. Micha, MD, is a gynecologic oncologist, attending physician at Hoag Hospital Cancer Center, and managing partner of Gynecologic Oncology Associates in Newport Beach, CA.

Cheri L. Graham, RN, is an experienced charge nurse who conducts clinical research for Gynecologic Oncology Associates and the Women's Cancer Research Foundation in Newport Beach, CA.

Mark A. Rettenmaier, MD, is a gynecologic oncologist, attending physician at Hoag Hospital Cancer Center, and a treating physician for Gynecologic Oncology Associates in Newport Beach, CA.

John V. Brown III, MD, is a gynecologic oncologist, attending physician at Hoag Hospital Cancer Center, and a treating physician for Gynecologic Oncology Associates in Newport Beach, CA.

Bram H. Goldstein, PhD, is a postdoctoral fellow at Gynecologic Oncologic Associates and the Women's Cancer Research Foundation in Newport Beach, CA.

## Notes

1. Lockwood, C. J. "Snatching the Ob/Gyn Physician-Scientist from the Verge of Extinction." *Contemporary OB/GYN* 107, no. 5 (2006): 312–315.
2. Jameson, S. "The Benefits and Challenges of Conducting Clinical Trials." *Community Oncology* 3, no. 2 (2006): 163–166.
3. Nyden, P. "Academic Incentives for Faculty Participation in Community-based Participatory Research." *Journal of General Internal Medicine* 18, no. 7 (2003): 576–585.
4. Magill, M. K., A. P. Catinella, L. Haas, and C. C. Hughes. "Cultures in Conflict: A Challenge to Faculty of Academic Health Centers." *Academic Medicine* 73, no. 8 (1998): 871–875.
5. Ibid.
6. Bridges, J. F. "Reconsidering the Role of Private Health Funds in Australia: A Dynamic Model." *Applied Health Economics and Health Policy* 2, no. 2 (2003): 109–117.
7. Gallin, E. K., S. M. Le Blancq, and Clinical Research Fellowship Program Leaders. "Launching a New Fellowship for Medical Students: The First Years of the Doris Duke Clinical Research Fellowship Program." *Journal of Investigative Medicine* 53, no. 2 (2005): 73–81.
8. Fisch, M. J., and E. Bruera (Editors). "Decision Making Towards the End of Life." *Handbook of Advanced Cancer Care*. Cambridge: Cambridge University Press, 2003.
9. Fulcher, C. D., and T. K. Gosselin-Acomb. "Distress Assessment: Practice Change through Guideline Implementation." *Clinical Journal of Oncology Nursing* 11, no. 6 (2007): 817–821.
10. Micha, J. P. "Expanding Research Infrastructure." *The Women's Oncology Review* 3, no. 2 (2003): 177–178.
11. Ley, T. J., and L. E. Rosenberg. "The Physician-Scientist Career Pipeline in 2005: Build It, and They Will Come." *Journal of the American Medical Association* 294, no. 11 (2005): 1343–1351.
12. Wells, K. B., A. Staunton, and K. C. Norris. "Building an Academic-Community Partnered Network for Clinical Services Research: The Community Health Improvement Collaborative (CHIC)." *Ethnicity & Disease* 16, no. 1 (2006): S3–S17.
13. Alleyne, J., and M. O. Jumaa. "Building the Capacity for Evidence-based Clinical Nursing Leadership: The Role of Executive Co-coaching and Group Clinical Supervision for Quality Patient Services." *Journal of Nursing Management* 15, no. 3 (2007): 230–243.
14. Micha, J. P. "Expanding Research Infrastructure."
15. Palmer, R. C., and L. A. Midgette. "Preventive Health Patient Education and Counseling: A Role for Medical Assistants?" *Journal of Allied Health* 37, no. 3 (2008): 137–143.
16. Walker, S. H., V. Ouellette, and V. Ridde. "How Can PhD Research Contribute to the Global Health Research Agenda?" *Canadian Journal of Public Health* 97, no. 2 (2006): 145–148.
17. Gladwin, J., R. A. Dixon, and T. D. Wilson. "Implementing a New Health Management Information System in Uganda." *Health Policy and Planning* 18, no. 2 (2003): 214–224.
18. Lorenzi, N. M., and R. T. Riley. "Organizational Issues = Change." *International Journal of Medical Information* 69, nos. 2–3 (2003): 197–203.
19. Jameson, S. "The Benefits and Challenges of Conducting Clinical Trials."
20. Micha, J. P. "Expanding Research Infrastructure."

21. Dyrbye, L. N., M. R. Thomas, and A. J. Mechaber. "Medical Education Research and IRB Review: An Analysis and Comparison of the IRB Review Process at Six Institutions." *Academic Medicine* 82, no. 7 (2007): 654–660.
22. Hudson, T. "Is Medical Research Doomed?" *Hospital Health Network* 71, no. 20 (1997): 40–44.
23. Matherlee, K. R. "The Outlook for Clinical Research: Impacts of Federal Funding Restraint and Private Sector Reconfiguration." *Academic Medicine* 70, no. 12 (1995): 1065–1072.
24. Quattrin, R., A. Zanini, and E. Nascig. "Level of Burnout among Nurses Working in Oncology in an Italian Region." *Oncology Nursing Forum* 33, no. 4 (2006): 815–820.

**Table 1**

List of Women's Cancer Research Foundation Publications (2003–2007)

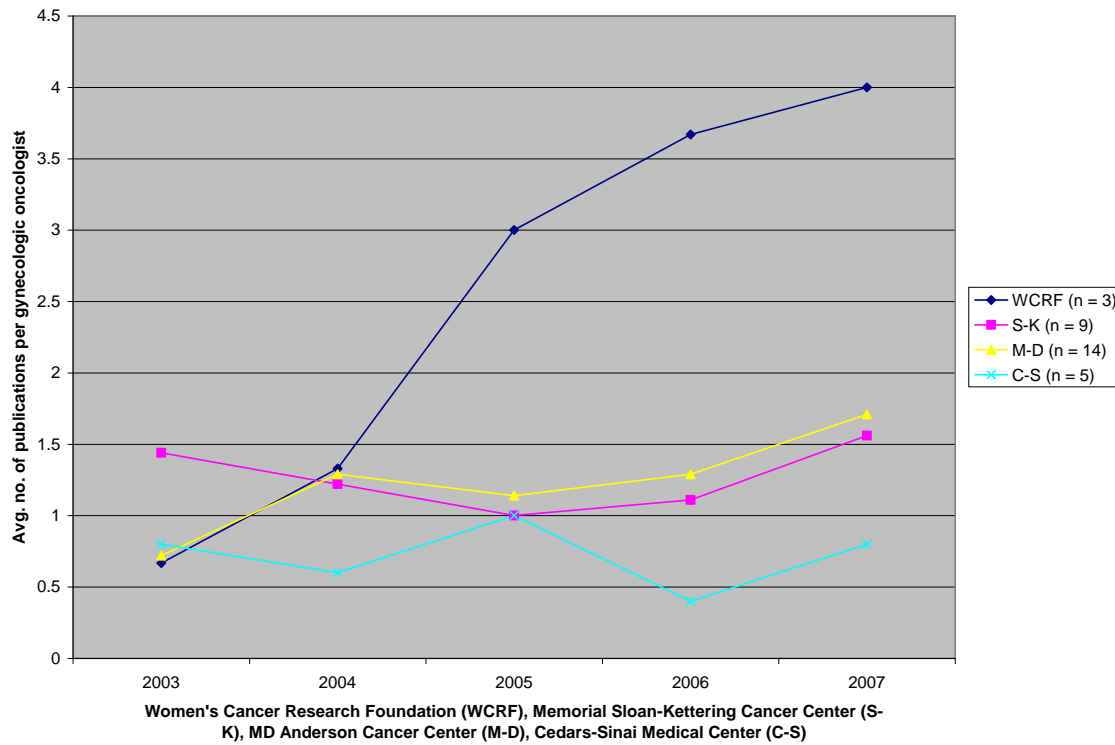
1. Brown, J. V., et al. "Three-Consecutive-Day Topotecan Is an Active Regimen for Recurrent Epithelial Ovarian Cancer." *Gynecologic Oncology* 88 (2003): 136–140.
2. Rettenmaier, M. A., et al. "Modified Vestibulectomy Is Inadequate Treatment for Secondary Vulvar Vestibulitis." *Journal of Gynecological Surgery* 19 (2003): 13–17.
3. Micha, J. P. "Expanding Research Infrastructure." *The Women's Oncology Review* 3 (2003): 177–178.
4. Micha, J. P., et al. "Long-term Survival in an Ovarian Cancer Patient with Brain Metastases: A Case Report." *Gynecologic Oncology* 92 (2004): 978–980.
5. Rettenmaier, M. A., et al. "Impact of Gynecologic Oncologists in the Care of Uterine Malignancies at a Community Hospital." *International Journal of Gynecological Cancer* 20 (2004): 57–63.
6. Micha, J. P., et al. "Pilot Study of Outpatient Paclitaxel, Carboplatin and Gemcitabine for Advanced Stage Epithelial Ovarian, Peritoneal, and Fallopian Tube Cancer." *Gynecologic Oncology* 94 (2004): 719–724.
7. Micha, J. P., et al. "Cecal Pelvic Transposition Following Total Pelvic Exenteration." *Gynecologic Oncology* 94 (2004): 589–592.
8. Brown, J. V., et al. "Laser Ablation of Surgical Margins Following Excisional Partial Vulvectomy for VIN: Effect on Recurrence." *Journal of Reproductive Medicine* 50 (2005): 345–350.
9. Rettenmaier, M. A., et al. "Greatly Elevated Serum CA-125 Level in a Patient with a Ruptured Endometrioma." *Journal of Gynecological Surgery* 21 (2005): 109–112.
10. Rettenmaier, M. A., et al. "Serous Psammocarcinoma of the Ovary: An Unusual Finding." *Gynecologic Oncology* 99 (2005): 510–511.
11. Micha, J. P., et al. "Experience with Single-agent Paclitaxel Consolidation Following Primary Chemotherapy with Carboplatin, Paclitaxel, and Gemcitabine in Advanced Ovarian Cancer." *Gynecologic Oncology* 96 (2005): 132–135.
12. Micha, J. P., et al. "Abdominal/Pelvic Coccidioidomycosis." *Gynecologic Oncology* 96 (2005): 256–258.
13. Brown, J. V., et al. "Gamma-Knife Radiosurgery for the Treatment of Ovarian Cancer Metastatic to the Brain." *Gynecologic Oncology* 97 (2005): 858–861.
14. Micha, J. P., et al. "Abraxane in the Treatment of Ovarian Cancer: The Absence of a Hypersensitivity Reaction." *Gynecologic Oncology* 100 (2005): 437–438.
15. Brown, J. V., et al. "Laser Ablation of Surgical Margins After Excisional Partial Vulvectomy for VIN." *Obstetrical & Gynecological Survey* 60 (2005): 584–585.
16. Micha, J. P., et al. "Spontaneous Bacterial Peritonitis Following Treatment for Cervical Carcinoma." *International Journal of Gynecological Cancer* 16 (2006): 908–911.
17. Micha, J. P., et al. "Surgery Alone or Surgery with a Combination Radiation or Chemo-Radiation for Management of Patients with Bulky Stage 1B2 Cervical Carcinoma." *International Journal of Gynecological Cancer* 16 (2006): 1147–1151.



18. Micha, J. P., et al. "A Rare Case of Coccygeal Endometriosis." *Obstetrics & Gynecology* 107 (2006): 1–2.
19. Rettenmaier, M. A., et al. "Recurrent Gestational Trophoblastic Disease Following Persistently Normal hCG titers: A Rare Occurrence." *American Journal of Clinical Oncology* 29 (2006): 1–2.
20. Micha, J. P., et al. "A Response to Batt: A Rare Case of Precoccygeal Endometriosis." *Obstetrics & Gynecology* 108 (2006): 213–214.
21. Micha, J. P., B. H. Goldstein, M. A. Rettenmaier, and J. V. Brown III. "Neo-vagina Reconstruction Utilizing the Bladder and Urethra Following Radical Radiation Therapy." *Journal of Gynecologic Surgery* 22 (2006): 73–75.
22. Micha, J. P., B. H. Goldstein, M. A. Rettenmaier, J. T. Caillouette, M. J. Fee, and J. V. Brown III. "Pelvic Radiation Necrosis and Osteomyelitis Following Chemo Radiation for Advanced Stage Vulvar and Cervical Carcinoma." *Gynecologic Oncology* 101 (2006): 349–352.
23. Rettenmaier, M. A., et al. "Lymphoepithelial Carcinoma of the Cervix: Review and Treatment Course." *Journal of Gynecologic Surgery* 21 (2005): 185–188.
24. Micha, J. P., B. H. Goldstein, M. A. Rettenmaier, and J. V. Brown III. "Ovarian Cancer Metastatic to the Breast." *Gynecologic Oncology* 102 (2006): 386–390.
25. Rettenmaier, M. A., et al. "Serous Endometrial Intraepithelial Carcinoma: Diagnosis and Clinical Management." *Journal of Gynecologic Surgery* 22 (2006): 69–72.
26. Rettenmaier, M. A., et al. "Vaginal Reconstruction Following Supra-Levator Total Pelvic Exenteration." *Gynecologic Oncology* 102 (2006): 397–399.
27. Micha, J. P., et al. "Extended Follow-Up with Single Agent Paclitaxel Consolidation/Maintenance Therapy in Advanced Ovarian Carcinoma." *Oncology* 71 (2006): 49–53.
28. Micha, J. P., B. H. Goldstein, D. Zusman, M. A. Rettenmaier, H. D. Epstein, and J. V. Brown III. "Malignant Pericardial Effusion Secondary to Ovarian Adenocarcinoma." *Journal of Reproductive Medicine* 52 (2007): 971–973.
29. Micha, J. P., et al. "A Precarious Case of Multiple Enlarged Arteriovenous Malformations in the Uterus." *Journal of Gynecologic Surgery* 23 (2007): 23–29.
30. Micha, J. P., et al. "A Rare Case of Low-Grade Pelvic Masses with Spindle Cell and Fibroblastic Proliferation." *Journal of Medical Case Reports* 1 (2007): 16–19.
31. Micha, J. P., et al. "Tuberculosis Mimicking Cervical Carcinoma." *European Journal of Gynaecological Oncology* 4 (2007): 316–318.
32. Micha, J. P., et al. "Retroperitoneal Schwannoma Presenting as a Gynecologic Mass: A Rare Case Report." *Journal of Gynecologic Surgery* 23 (2007): 157–162.
33. Brown, J. V., et al. "Rapid Manifestation of CNS Metastatic Disease in a Cervical Carcinoma Patient: A Case Report." *Oncology* 73 (2007): 273–276.
34. Micha, J. P., et al. "Subclavian Artery Puncture Repair with Angio-Seal Deployment." *Gynecologic Oncology* 104 (2007): 761–763.
35. Micha, J. P., et al. "Pilot Study of Outpatient Paclitaxel, Carboplatin and Bevacizumab for Advanced Stage Epithelial Ovarian, Peritoneal, and Fallopian Tube Cancer." *International Journal of Gynecological Cancer* 17 (2007): 771–776.

Figure 1

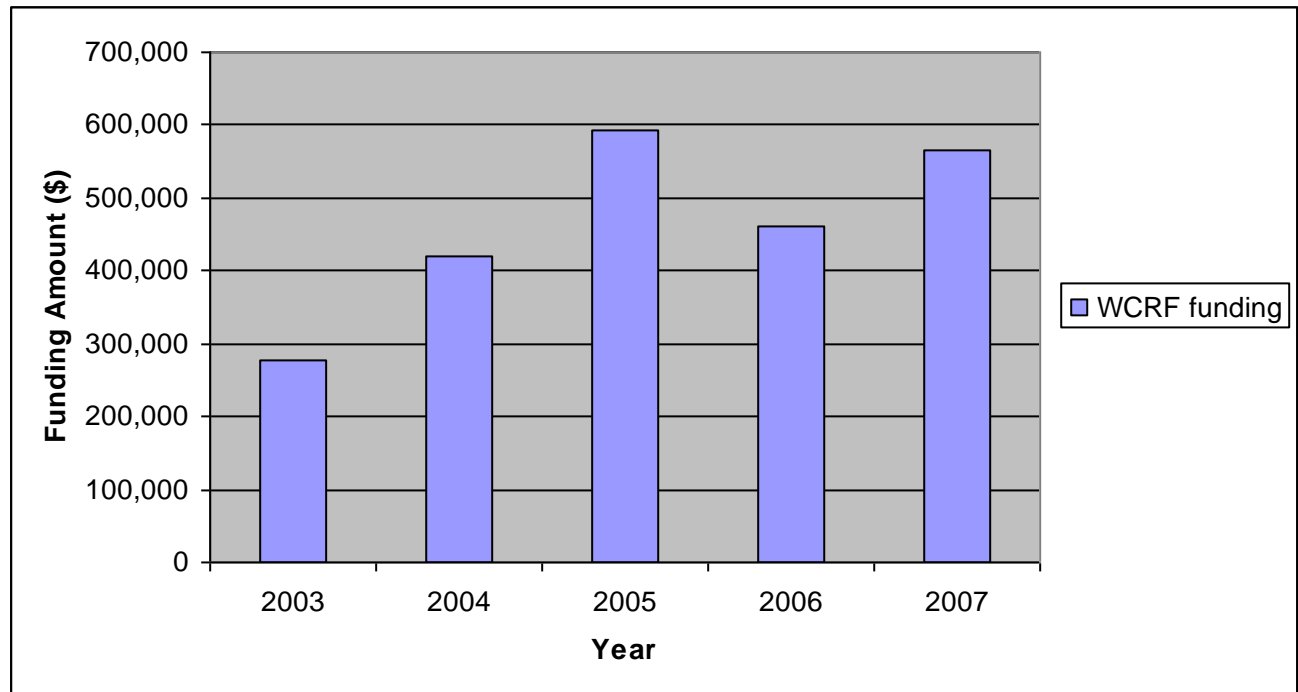
Average Number of Gynecologic Oncologist First-Author Publications at the Individual Cancer Centers



*Note:* This graph was calculated by tallying the number of first-author gynecologic oncology publications for each institution ([www.pubmed.gov](http://www.pubmed.gov)) and dividing the statistic by the number of gynecologic oncology physicians ( $n$ ) within the specific institution.

**Figure 2**

Annual WCRF Grant and Public Funding (2003–2007)



**Figure 3**

Flowchart Exhibiting WCRF Research Model Components

